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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,483	10/07/2004	Hiroyuki Miyata	0283-0200PUS1	7464

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EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
05/18/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/510,483	MIYATA ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the species of Example 1 shown on pages 57-60 wherein the enzyme is a lipase and the specific penatonate and specific pentanoic acid for the reactant and product, respectively, in the reply filed on 2/12/07 is acknowledged.

A search of the literature and patents revealed the various compound and hydrolase species. Therefore, the specie elections are withdrawn.

Claims 1-11 are presented for examination.

Specification

The use of the trademarks CHIRAZYME and AMANO PS has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, 121 or 365(c), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application

data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims recite a process for resolving a racemic mixture containing an N-substituted beta-amino acid or an N-substituted-2-homopipecolic acid by selectively hydrolyzing one enantiomer with a hydrolase. Claim 2 further defines the hydrolase as a lipase, and esterase or a protease. Claims 3 and 11 are directed to a lipase that is "originated" from Candia antartica.

Whether a specification complies with the written description requirement of § 112, first paragraph, is a question of fact *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111,

1116 (Fed. Cir. 1991); *Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985). To fulfill the written description requirement, a specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, the written description requirement is satisfied "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of the desired hydrolase, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, an adequate written description of the desired hydrolase requires more than a mere statement that it is part of the invention and a general statement that any hydrolase, in particular a protease, a lipase or an esterase, can carry out the claimed invention; what is required is a description of the hydrolase itself.

However, the as-filed specification provides no specific description for the vast majority of the claim-encompassed hydrolases that are capable of catalyzing the claimed resolution. The specification discloses that lipases, esterases and proteases can be isolated from yeast or bacteria may catalyze the claimed reaction. Yet, the specification only describes lipase from *Candida antartica* (Chirazyme™) and a Pseudomonas lipase from Amano PS which applicant actually

demonstrates as having the required stereoselective hydrolytic activity. The use of the term "originating" in claims 3 and 9 implies that the preparation of a multitude of genetically recombined organisms that produce a lipase with the desired activity is disclosed by the as-filed specification. Therefore, the claims encompass the use of numerous potential hydrolases to carry out the claimed reaction. However, there is no specific written description for the use or preparation of hydrolases other than lipase from *Candida antartica* (Chirazyme™) and a Pseudomonas lipase (Amano PS™) which applicant actually demonstrates as having the required stereoselective hydrolytic activity. Moreover, the sole example using the lipase from *Candida antartica* and a Pseudomonas lipase from Amano PS as a biocatalyst does not provide a representative sample of the hydrolases encompassed by the claims, given the huge variation in catalytic properties of hydrolases that are encompassed by the current broad claim language. Because the claims encompass a multitude of hydrolases neither contemplated nor disclosed by the as-filed disclosure, it is clear that applicant was not in possession of the full scope of the claimed subject matter at the time of filing.

Claims 1, 2, and 4-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for resolving a racemic mixture containing an N-aryl substituted beta-amino acid or an N-aryl ubstituted-2-homopipecolic acid by selectively hydrolyzing one enantiomer with a hydrolase with is a lipase from C. antartica or from Pseudomonas Amano PS, does not reasonably provide enablement for the a process for resolving a racemic mixture containing an N-aryl substituted beta-amino acid or an N-aryl substituted-2-homopipecolic acid by selectively hydrolyzing one enantiomer with any hydrolase.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected,

to use the invention commensurate in scope with these claims. The claims are drawn to a process for resolving a racemic mixture containing an N-aryl substituted beta-amino acid or an N-aryl substituted-2-homopipecolic acid by selectively hydrolyzing one enantiomer with a hydrolase. The specification show that lipases from C. antartica and Pseudomonas Amano PS are capable of catalyzing the stereoselective ester hydrolysis of beta-amino acids or 2-homopipecolic acids having N-aryl substitution.

However, there is no disclosure by the specification or the prior art of other hydrolases that are capable of carrying out the claimed reaction. In fact, the prior art demonstrates that the selection of hydrolases that can carry out ester hydrolysis is unpredictable. For example, Dicosimo et al. (US 5,928,933; disclosed in the IDS filed 10/7/04) discloses the resolution of racemic mixtures of N-(alkoxycarbonyl)_4-keto-D,L-proline alkyl esters with Candida antartica fraction B. Dicosimo et al. shows in Tables 2-7, that the ability of other lipases, proteases or esterases to carry out the reaction is not predictable. Many of the hydrolases were unable to catalyze the stereoselective hydrolysis while other hydrolases had low racemate conversion or yielded a product with a low e.e. In view of the lack of any specific guidance with respect to identifying other hydrolases that can catalyze the claimed reaction, the skilled artisan would expect to have to undertake a trial and error process such as screening to determine which of the multitude of hydrolases by the claims would be amenable to the techniques disclosed in the instant application. Such a trial and error process clearly amounts to undue experimentation.

The limited showing of two hydrolases having a particular stereoselective enzymatic activity is not sufficient to enable a claim drawn to the stereoselective hydrolysis by any possible hydrolase because the art of Enzymology is too unpredictable. The determination of how enzymes with

interact with substrates requires an understanding of the catalytic mechanism and the characterization of the active site and the topology of the enzyme in order to understand how various molecules bind to the enzyme and/or be chemically changed by the enzyme in question. At the time of the invention, stereoselective ester hydrolysis in general was known. However, as shown by the Dicosimo patent, the interaction of hydrolases with a racemic mixture is not predictable.

There is no method that predicts what hydrolases will catalyze the desired stereoselective hydrolysis of the claimed N-aryl substituted substrates as described in the specification. It is well known in the art that enzymatic activity and specificity is complex. There is no predictable way for a skilled artisan to know in advance what hydrolases will have the desired stereoselective activity as set forth in the instant application. The limited disclosure cannot be extrapolated by the skilled artisan to predict when the disclosure is enabling for identifying said stereoselective hydrolases. It would require one of ordinary skill in the art undue experimentation to predict what hydrolases will catalyze the desired stereoselective hydrolysis of the claimed N-aryl substituted substrates according to the directions of the instant disclosure. Thus, claims 1, 2 and 4-10 are not commensurate in scope with the enabling disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 8 recite the limitation "it" in lines 22 and 11, respectively, of each claim. There is insufficient antecedent basis for this limitation in each claim.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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